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Dr. Joshua Lederberg Office of the President The Rockefeller University 1230 York Ave. New York, NY 10021-6399

Dear Dr. Lederberg:

I am rarely reminded - and others are even less so - of the "ancient problems" of Neurospora heterokaryons and the phenomena of nuclear adaptation. Your inquiry was at least as much of a surprise as a pleasure. Unfortunately, I have done little else along these lines since my thesis work on the pan - pan m competition in Neurspora, and I have little more of substance or speculation to offer. A somewhat more extended discussion of heterokaryosis and its peculiar consequences as a genetic system was published in a review in Vol. II of The Fungi - An Advanced Treatise, edited by Ainsworth and Sussman in 1966 (Chapter 17, pp. 567-588; Academic Press).

Since then, I have two items, enclosed, that may interest you. One is on reversion and transformation in Neurospora. It addresses the reasons it might be impossible to propagate a homokaryotic transformant, an issue you raise in your letter. To address the specific question about maladaptive traits (e.g., tRNA suppressors in homokaryotic form) that might preclude cloning of revertants, this issue never arose in yours or my early work, because the revertants could be isolated in pure form. But I am sure that the situation you suggest arises frequently and is almost necessarily ignored.

The other item is one on tests for suppressible alleles of a gene using heterokaryons that contain a nominally dominant tRNA suppressor. Such tests do not often work, owing, I believe, to insufficient dosage of the suppressor tRNA or of the suppressible mRNA in such heterokaryons. This may in fact be the sort of information you were seeking: suppressors arising in heterokaryotic mycelia have an uphill battle to assert themselves, and may only rarely be seen for that reason.

Thank you for your letter, with best wishes.

Sincerely yours,

Rowland H. Davis

Professor of Molecular Genetics